

Initial REMS approval: 08/2015

**NDA 22526 Addyi™ (flibanserin)**

Serotonin 1A receptor agonist and a Serotonin 2A receptor antagonist

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**RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

**I. GOAL(s)**

The goal of the Addyi REMS is to mitigate the increased risk of hypotension and syncope associated with Addyi due to an interaction with alcohol by:

- Ensuring prescribers and pharmacists are educated about the increased risk of hypotension and syncope associated with Addyi due to an interaction with alcohol and the need to counsel patients about this risk.
- Informing patients of the increased risk of hypotension and syncope associated with Addyi due to an interaction with alcohol.

**II. ELEMENTS**

**A. Elements To Assure Safe Use**

1. Healthcare providers who prescribe Addyi for outpatient use must be specially certified.
  - a. To become specially certified to prescribe Addyi in the Addyi REMS Program, healthcare providers must:
    - i. Review the Prescribing Information (PI) for Addyi.
    - ii. Review the *Addyi REMS Program Prescriber and Pharmacy Training* and successfully complete the *Addyi REMS Program Knowledge Assessment*.
    - iii. Enroll in the Addyi REMS Program by completing the *Addyi REMS Program Prescriber Enrollment Form*.
  - b. As a condition of certification, prescribers must:
    - i. Counsel patients about the increased risk of hypotension and syncope associated with Addyi due to an interaction with alcohol, using the *Addyi REMS Program Patient-Provider*

*Agreement Form*. Maintain the completed *Addyi REMS Program Patient-Provider Agreement Form* in the patient's records and provide the patient with the portion of the *Addyi REMS Program Patient-Provider Agreement* designated for patient receipt.

- ii. Report any adverse events of hypotension or syncope where an interaction with alcohol cannot be ruled out to Sprout Pharmaceuticals.
- c. Sprout Pharmaceuticals must:
  - i. Ensure that healthcare providers who prescribe Addyi for outpatient use are specially certified, in accordance with the requirements described above.
  - ii. Ensure that healthcare providers can complete the enrollment and certification processes in the Addyi REMS Program online, by email, by fax, or by phone..
  - iii. Ensure that healthcare providers are notified when they have been certified in the Addyi REMS Program.
  - iv. Maintain a validated, secure database of healthcare providers who are certified to prescribe Addyi in the Addyi REMS Program.
  - v. Ensure that healthcare providers meet the REMS requirements and de-certify healthcare providers who do not maintain compliance with REMS requirements.
  - vi. Ensure that certified prescribers are provided access to the database of certified pharmacies.
  - vii. Provide the *Addyi REMS Program Prescriber Enrollment Form*, *Addyi REMS Program Prescriber and Pharmacy Training*, *Addyi REMS Program Knowledge Assessment*, and the PI to healthcare providers who (1) attempt to prescribe Addyi and are not yet certified, or (2) inquire about how to become certified.

The following materials are part of the REMS and are appended:

- [\*Addyi REMS Program Prescriber Enrollment Form\*](#)
- [\*Addyi REMS Program Prescriber and Pharmacy Training\*](#)
- [\*Addyi REMS Program Knowledge Assessment\*](#)
- [\*Addyi REMS Program Website screenshots\*](#)
- [\*Addyi REMS Program Patient-Provider Agreement Form\*](#)

2. Pharmacies that dispense Addyi must be specially certified.

- a. To become specially certified to dispense Addyi in the Addyi REMS Program, pharmacies must:
  - i. Designate an authorized representative to complete the enrollment and certification processes by submitting the completed appropriate pharmacy enrollment form on behalf of the pharmacy.
    - 1) Outpatient Pharmacy:
      - *Addyi REMS Program Multiple Location Pharmacy Enrollment Form*

- *Addyi REMS Program Individual Location Pharmacy Enrollment Form*

- 2) Inpatient Pharmacy: *Addyi REMS Program Inpatient Pharmacy Enrollment Form*
- ii. Ensure that the authorized representative oversees implementation and compliance with the Addyi REMS Program requirements by doing the following:
    - 1) Review the *Addyi REMS Program Prescriber and Pharmacy Training* and the PI and successfully complete the *Addyi REMS Program Knowledge Assessment*.
    - 2) Ensure all relevant staff involved in the dispensing of Addyi are trained on the Addyi REMS Program requirements using the *Addyi REMS Program Prescriber and Pharmacy Training* and maintain a record of training.
    - 3) Put processes and procedures in place to ensure that prior to dispensing Addyi, the outpatient pharmacy verifies the prescriber is certified in the Addyi REMS Program and counsels the patient to avoid alcohol use with Addyi.
    - 4) Ensure all relevant staff involved in the dispensing of Addyi understand the importance of reporting any adverse event of hypotension and syncope where an interaction with alcohol cannot be ruled out to Sprout Pharmaceuticals or MedWatch.
    - 5) Maintain appropriate documentation that all processes and procedures are in place and are being followed for the Addyi REMS Program and provide such documentation upon request to Sprout Pharmaceuticals, FDA, or a designated third party.
    - 6) Comply with audits by Sprout Pharmaceuticals or a designated third party and inspections by FDA to ensure that all processes and procedures are in place and are being followed for the Addyi REMS Program.
  - b. As a condition of certification:
    - i. Outpatient pharmacies:
      - 1) Must recertify in the Addyi REMS Program if the pharmacy designates a new authorized representative.
      - 2) A pharmacy that supports electronic communication verification with the Addyi REMS Program system must:
        - a) Ensure the pharmacy enables its pharmacy management system to support communication with the Addyi REMS Program system, using established telecommunication standards, and runs the standardized validation test transaction to validate the system enhancements.
        - b) Dispense Addyi to patients only after obtaining a predispose authorization (PDA) by processing each prescription through its pharmacy management system to electronically verify the prescriber is certified in the Addyi REMS Program.
        - c) Prior to dispensing, counsel patients to avoid alcohol use with Addyi. .
      - 3) A pharmacy that does NOT support electronic telecommunication verification with the Addyi REMS Program system must:

- a) Dispense Addyi to patients only after obtaining authorization by calling the REMS Program Support Center to verify the prescriber is certified in the Addyi REMS Program.
  - b) Prior to dispensing, counsel patients to avoid alcohol use with Addyi.
- ii. Inpatient Pharmacies must:
  - 1) Recertify in the Addyi REMS Program if the pharmacy designates a new authorized representative.
  - 2) Dispense Addyi only for inpatient use unless the pharmacy is enrolled as an outpatient pharmacy and can comply with the requirements under 2(b)(i).
- c. Sprout Pharmaceuticals must:
  - i. Ensure that pharmacies that dispense Addyi are specially certified, in accordance with the requirements described above.
  - ii. Ensure that pharmacies can complete the certification and enrollment processes in the Addyi REMS Program online, by email, by fax, or by phone.
  - iii. Ensure that pharmacies are notified when they have been certified by the Addyi REMS Program.
  - iv. Verify every 2 years that the authorized representative's name and contact information corresponds to that of the current designated authorized representative for the certified pharmacy. If different, the pharmacy will be required to re-certify with a new authorized representative.

The following materials are part of the REMS and are appended:

- *Addyi REMS Program Multiple Location Pharmacy Enrollment Form*
- *Addyi REMS Program Individual Location Pharmacy Enrollment Form*
- *Addyi REMS Program Inpatient Pharmacy Enrollment Form*
- *Addyi REMS Program Prescriber and Pharmacy Training*
- *Addyi REMS Program Knowledge Assessment*

## **B. Implementation System**

- 1. Sprout Pharmaceuticals must ensure that Addyi is only distributed to certified pharmacies by:
  - a. Ensuring that wholesalers/distributors who distribute Addyi comply with the program requirements for wholesalers/distributors. The authorized wholesalers/distributors must:

- i. Put processes and procedures in place to verify, prior to distributing Addyi, that the pharmacy is certified using the validated, secure database provided by the Addyi REMS Program.
    - ii. Train all relevant staff on the Addyi REMS Program requirements.
    - iii. Comply with audits by Sprout Pharmaceuticals or a designated third party and inspections by FDA to ensure that all processes and procedures are in place and are being followed for the Addyi REMS Program. In addition, wholesalers/distributors must maintain appropriate documentation and make it available for audits.
    - iv. Provide distribution data to Sprout Pharmaceuticals.
  - b. Ensuring that authorized wholesalers/distributors maintain distribution records of all shipments of Addyi and provide the data to Sprout Pharmaceuticals.
2. Sprout Pharmaceuticals must audit the wholesalers/distributors within 60 calendar days after each wholesaler/distributor is authorized to distribute Addyi in order to ensure that all processes and procedures are in place and functioning to support the requirements of the Addyi REMS Program. Sprout Pharmaceuticals must ensure the authorized wholesalers/distributors meet the REMS requirements and institute corrective action for wholesalers/distributors who do not maintain compliance with the REMS requirements.
  3. Sprout Pharmaceuticals must maintain a validated, secure database of pharmacies that are certified to dispense Addyi in the Addyi REMS Program.
  4. Sprout Pharmaceuticals must maintain records of Addyi distribution and dispensing, certified prescribers, certified pharmacies, and authorized wholesalers/distributors to meet the REMS requirements.
  5. Sprout Pharmaceuticals must ensure that the pharmacies and authorized wholesalers/distributors meet the REMS requirements and will de-certify pharmacies and authorized wholesalers/distributors who do not maintain compliance with the REMS requirements.
  6. Sprout Pharmaceuticals must maintain an Addyi REMS Support Center (1-844-233-9415) and Addyi REMS Program Website ([www.AddyiREMS.com](http://www.AddyiREMS.com)). The REMS Program Website must include the option to print the PI, Medication Guide, and Addyi REMS materials. The Addyi product website for consumers and healthcare providers ([www.Addyi.com](http://www.Addyi.com)) must include a prominent REMS-specific link to the Addyi REMS Program Website.
  7. Sprout Pharmaceuticals must ensure that within 30 calendar days of REMS approval the REMS materials listed in or appended to the Addyi REMS document are available through the Addyi REMS Program Website or by calling the Addyi REMS Support Center.
  8. Sprout Pharmaceuticals must monitor the certified pharmacies to ensure the requirements of the Addyi REMS Program are being met. Sprout Pharmaceuticals must institute corrective action if noncompliance is identified.
  9. Sprout Pharmaceuticals must audit 100 certified pharmacies or 1% of certified pharmacies, whichever is greater, within 180 calendar days after the pharmacy places its first order of Addyi to ensure that all processes and procedures are in place and functioning to support the requirements of the Addyi

REMS Program. The certified pharmacies will also be included in Sprout Pharmaceuticals' ongoing annual audit plan. Sprout Pharmaceuticals must institute corrective action for certified pharmacies who do not maintain compliance with the REMS requirements.

10. Sprout Pharmaceuticals must take reasonable steps to improve implementation of and compliance with the requirements in the Addyi REMS Program based on monitoring and evaluation of the Addyi REMS Program.

### **III. Timetable for Submission of Assessments**

Sprout Pharmaceuticals must ensure FDA receives REMS assessments 6 months and 12 months from the date of the initial approval of the REMS (August 18, 2015) and annually thereafter on or before the anniversary date of the initial REMS approval. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 calendar days before the assessment due date.